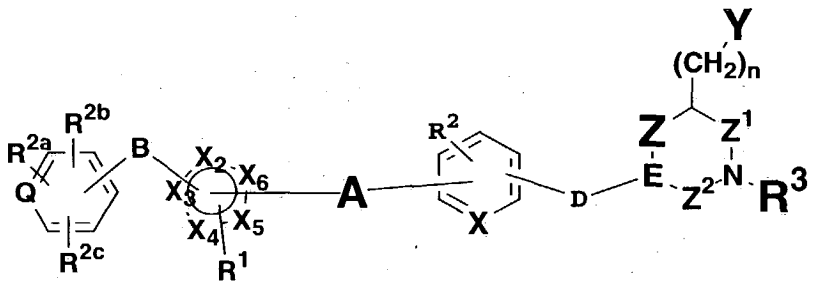
What is claimed is:

1. A compound having the structure



wherein Z^1 is $(CH_2)_q$ or C=O;

Z^2 is $(CH_2)_p$ or C=O;

D is -CH= or C=O or $(CH_2)_m$ where m is 0, 1, 2 or 3;

n = 0, 1 or 2; p = 1 or 2; q = 0, 1 or 2;

Q is C or N;

A is $(CH_2)_x$ where x is 1 to 5; or A is $(CH_2)_x^1$, where x^1 is 1 to 5, with an alkenyl bond or an alkynyl bond embedded anywhere in the chain; or A is $-(CH_2)_x^2-O-(CH_2)_x^3-$ where x^2 is 0 to 5 and x^3 is 0 to 5, provided that at least one of x^2 and x^3 is other than 0;

B is a bond or is $(CH_2)_x^4$ where x^4 is 1 to 5;

X is CH or N;

X_2 is C, N, O or S;

X_3 is C, N, O or S;

X_4 is C, N, O or S;

X_5 is C, N, O or S;

X_6 is C, N, O or S;

provided that at least one of X_2, X_3, X_4 X_5 and X_6 is N; and at least one of X_2, X_3, X_4 X_5 and X_6 is C;

R^1 is H or alkyl;

R^2 is H, alkyl, alkoxy, halogen, amino or substituted amino;

R^{2a}, R^{2b} and R^{2c} may be the same or different and are selected from H, alkyl, alkoxy, halogen, amino, substituted amino or cyano;

R^3 is selected from H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroaryl-heteroarylalkyl, alkylcarbonylamino, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylalkenyl, cycloheteroalkyl-heteroarylalkyl; hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, arylheteroarylalkyl, arylalkylarylalkyl, aryloxyarylalkyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylsulfinylarylcarbonyl, arylthioarylcarbonyl, alkoxycarbonylaryloxycarbonyl, arylalkenyloxycarbonyl, heteroaryloxyarylalkyl, aryloxyarylcarbonyl, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, heteroaryl-heteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylalkenyl, cycloheteroalkyl-heteroarylalkyl; hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, arylheteroarylalkyl, arylalkylarylalkyl, aryloxyarylalkyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylsulfinylarylcarbonyl, arylthioarylcarbonyl, alkoxycarbonylaryloxycarbonyl, arylalkenyloxycarbonyl, heteroaryloxyarylalkyl, aryloxyarylcarbonyl, aryloxyarylalkyloxycarbonyl, arylalkenyloxycarbonyl, arylalkylcarbonyl, aryloxyalkyloxycarbonyl,

arylalkylsulfonyl, arylthiocarbonyl, arylalkenylsulfonyl, heteroarylsulfonyl, arylsulfonyl, alkoxyarylalkyl, heteroarylalkoxycarbonyl, arylheteroarylalkyl, alkoxyarylcarbonyl, aryloxyheteroarylalkyl, heteroarylalkyloxyarylalkyl, arylarylalkyl, arylalkenylarylalkyl, arylalkoxyarylalkyl, arylcarbonylarylalkyl, alkylaryloxyarylalkyl, arylalkoxycarbonylheteroarylalkyl, heteroarylarylalkyl, arylcarbonylheteroarylalkyl, heteroaryloxyarylalkyl, arylalkenylheteroarylalkyl, arylaminoarylalkyl, aminocarbonylarylarylalkyl;

E is CH or N;

Z is $(CH_2)_x^5$ where x^5 is 0 (a single or a double bond), 1 or 2, or Z is $(CH_2)_x^6$ where x^6 is 2 to 5, where $(CH_2)_x^6$ includes an alkenyl (C=C) bond embedded within the chain or Z is $-(CH_2)_x^7-O-(CH_2)_x^8-$ where x^7 is 0 to 4 and x^8 is 0 to 4;

$(CH_2)_x$, $(CH_2)_x^1$, $(CH_2)_x^2$, $(CH_2)_x^3$, $(CH_2)_x^4$, $(CH_2)_x^5$, $(CH_2)_x^6$, $(CH_2)_x^7$, $(CH_2)_x^8$, $(CH_2)_m$, $(CH_2)_n$, $(CH_2)_p$ and $(CH_2)_q$ may be optionally substituted;

Y is CO_2R^4 where R^4 is H or alkyl, or a prodrug ester, or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure $P(O)(OR^{4a})R^5$ where R^{4a} is H or a prodrug ester, R^5 is alkyl or aryl, or a phosphonic acid of the structure $P(O)(OR^{4a})_2$;

including all stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof.

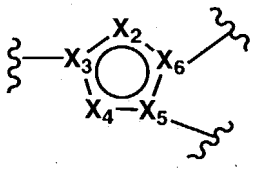
2. The compound as defined in Claim 1 wherein X is CH.

3. The compound as defined in Claim 1 wherein A is $-CH_2)_x^2-O-$.

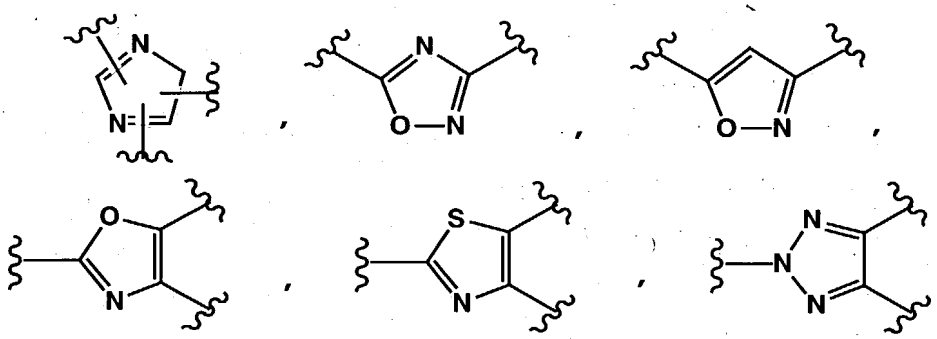
4. The compound as defined in Claim 1 wherein Q is C.

5. The compound as defined in Claim 1 wherein B is a bond.

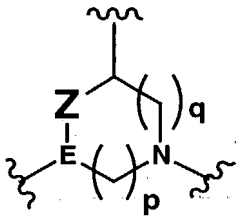
6. The compound as defined in Claim 1 wherein



is



7. The compound as defined in Claim 1 wherein



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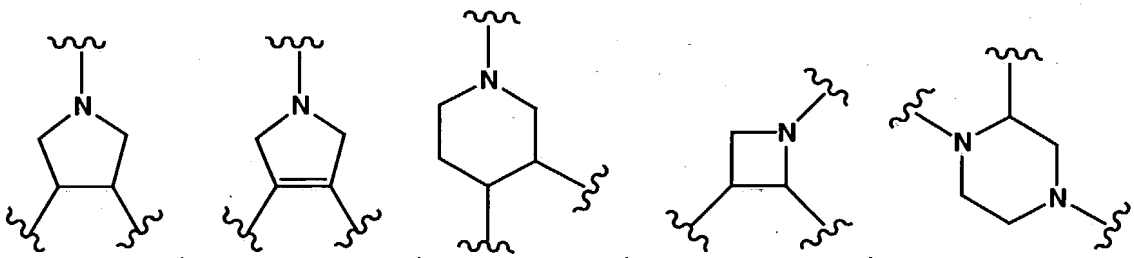
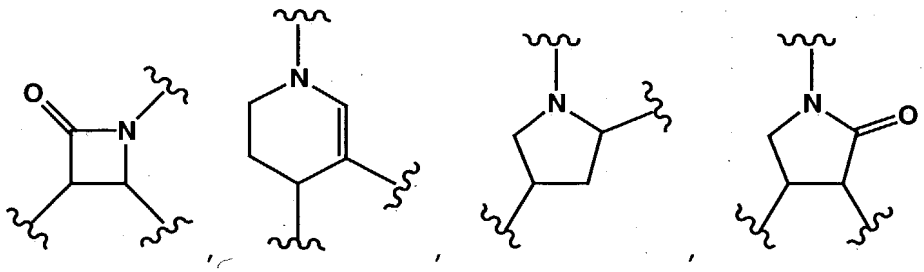
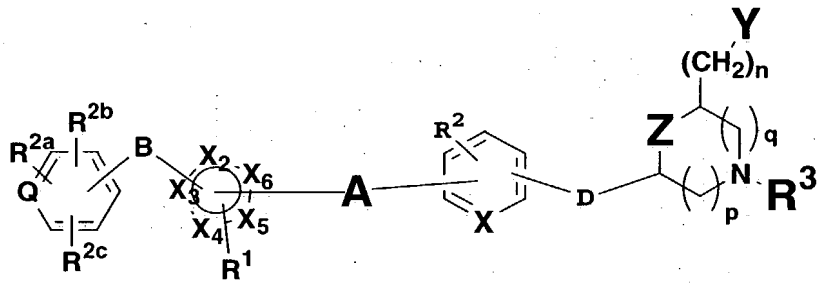


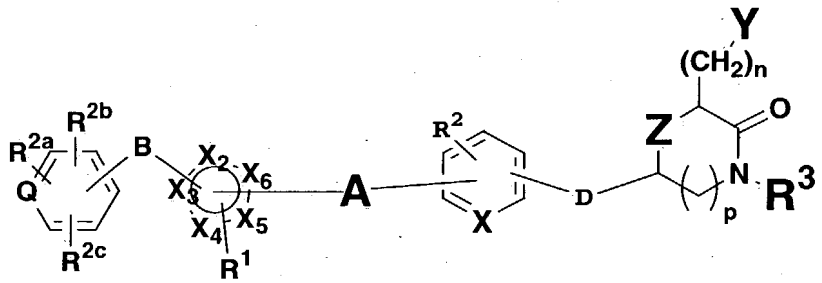


8. The compound as defined in Claim 1 having the structures

Ia



Ib



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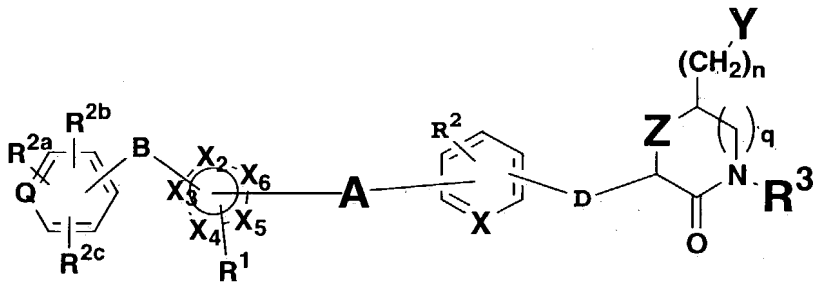

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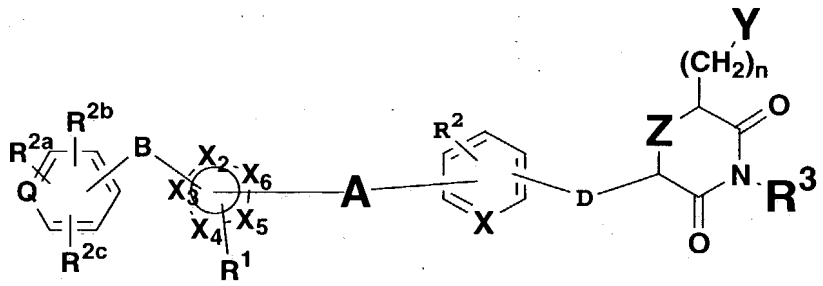
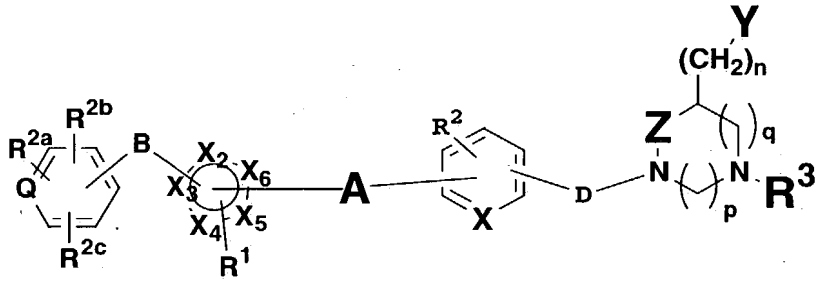
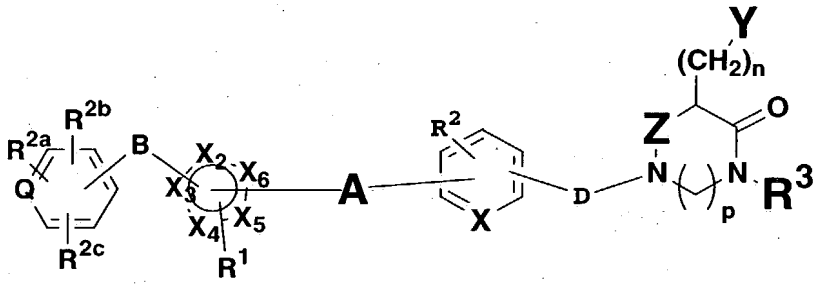


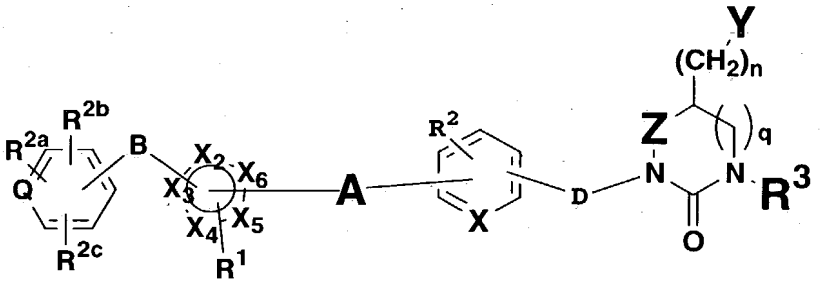
Ie



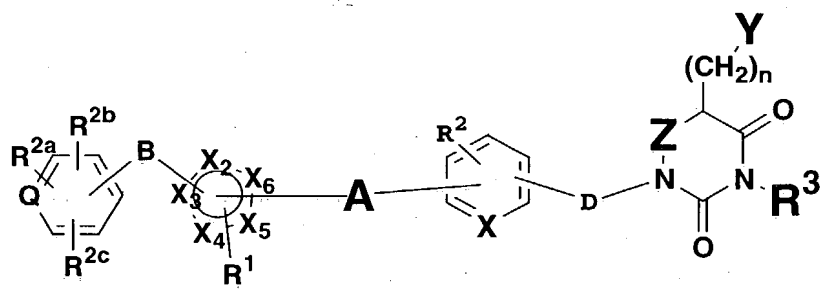
If



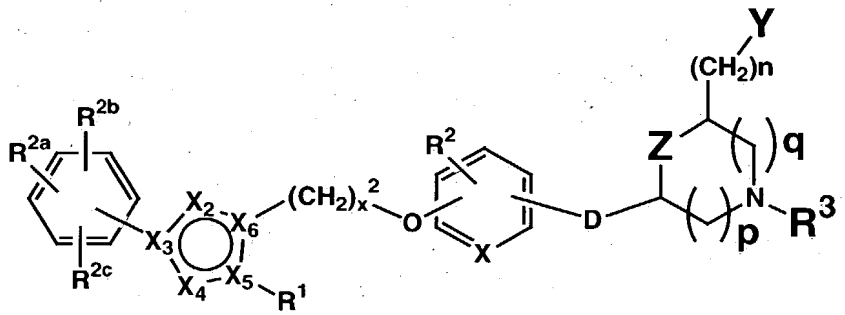
Ig



Ih

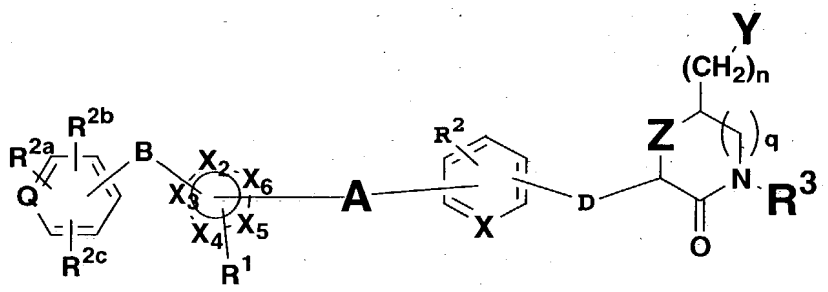


9. The compound as defined in Claim 1 having the structure



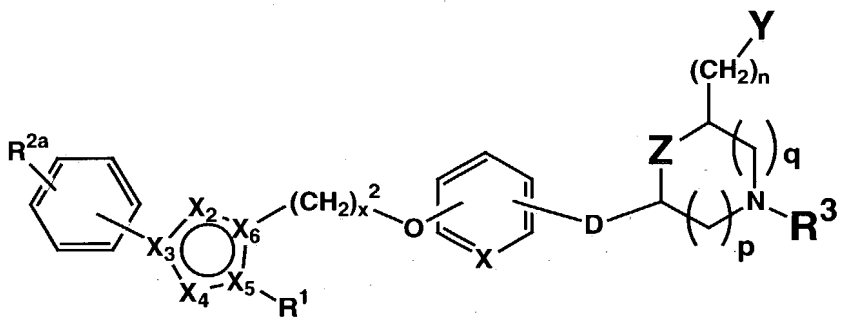
where X is CH.

IB

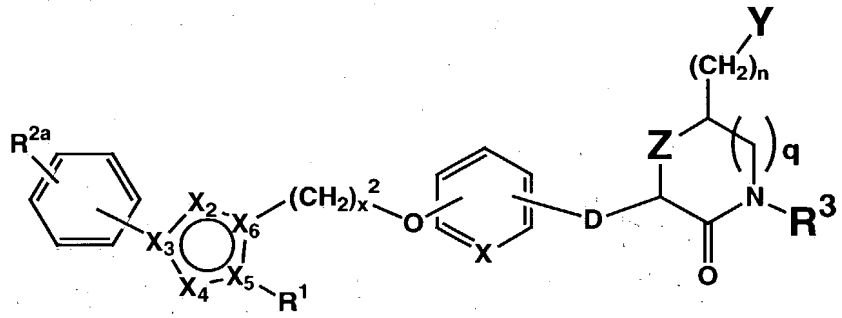


where X is CH.

10. The compound as defined in Claim 1 having the structure

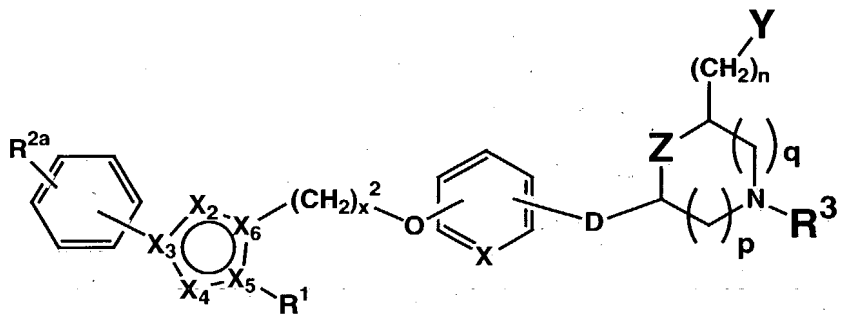


where X is CH.



where X is CH, q = 0, and Z is a single bond.

11. The compound as defined in Claim 1 having the structure



wherein

R^1 is alkyl;

R^{2a} is alkyl, alkoxy or halogen;

x^2 is 1 to 3;

D is -CH= or $(CH_2)_m$ where m is 0 or $(CH_2)_m$ is CH_2 or CH-alkyl;

X is CH;

X_2, X_3, X_4, X_5, and X_6 represent a total of 1, 2 or 3 nitrogens;

$(CH_2)_n$ is a bond or CH_2;

p is 1;

Z is a bond;

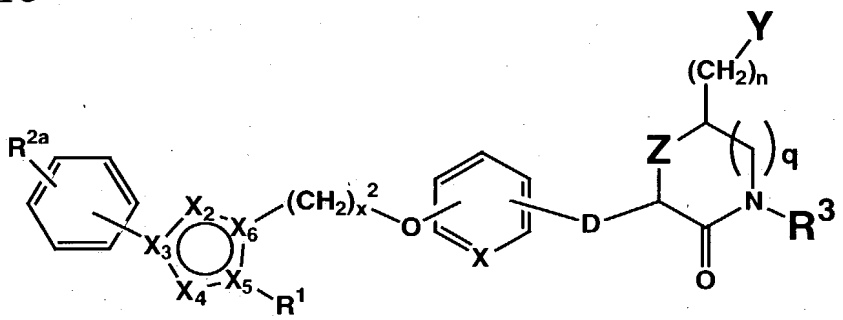
q is 1;

R^3 is alkoxycarbonyl, aryl, heteroaryl, aryloxycarbonyl or arylalkyl;

Y is CO_2R^4; and

n is 0.

12. The compound as defined in Claim 1 having the structure



wherein R^1 is alkyl;

R^{2a} is alkyl, alkoxy or halogen,

x^2 is 1 to 3;

D is -CH= or $(CH_2)_m$ where m is 0 or $(CH_2)_m$ is CH_2 or CH-alkyl;

X is CH;

X_2, X_3, X_4, X_5, and X_6 represent a total of 1, 2 or 3 nitrogens;

$(CH_2)_n$ is a bond or CH_2;

Z is a bond,

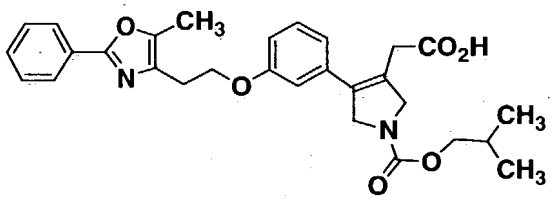
q is 0 or 1;

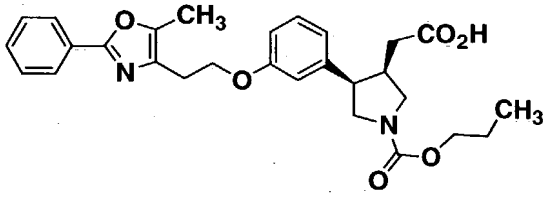
R^3 is alkoxycarbonyl, aryl, heteroaryl, aryloxycarbonyl or arylalkyl;

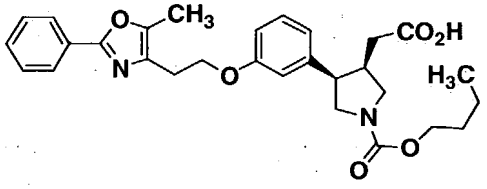
Y is CO_2R^4; and

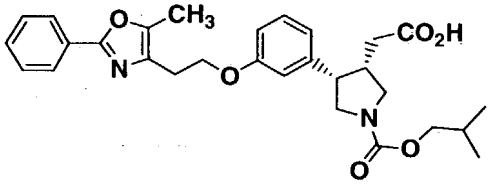
n is 0.

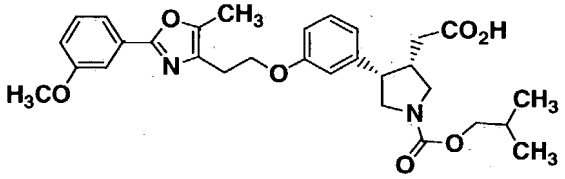
13. The compound as defined in Claim 1 having the structure

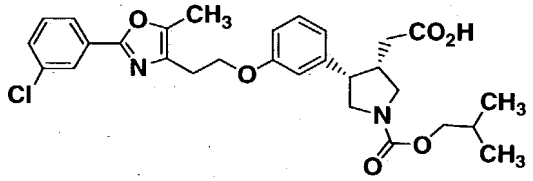


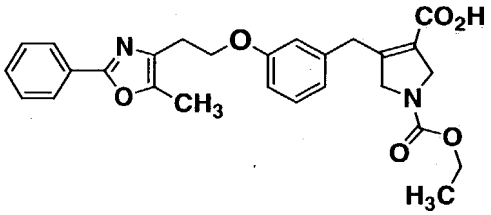


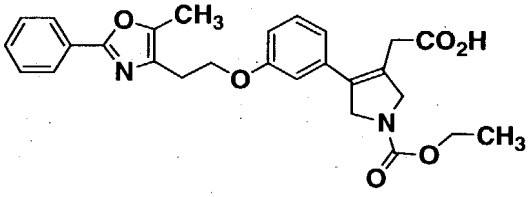


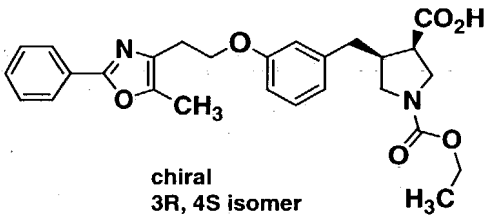


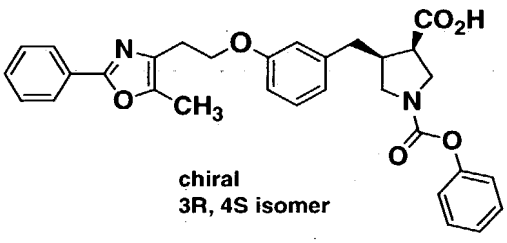


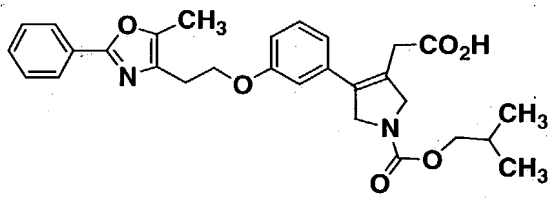


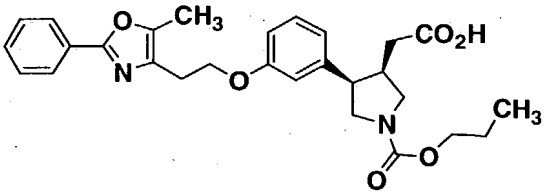


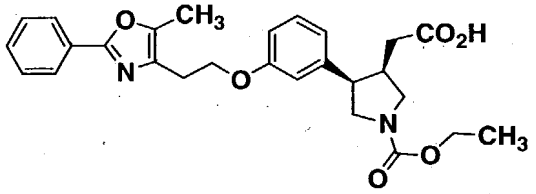


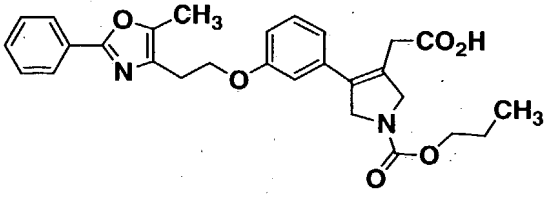

chiral
3R, 4S isomer

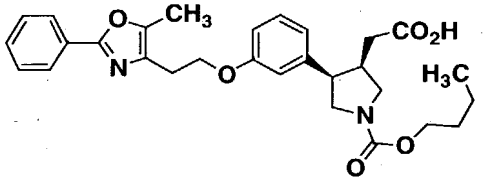

chiral
3R, 4S isomer

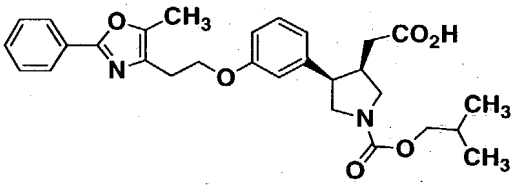


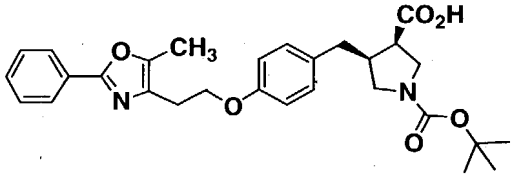


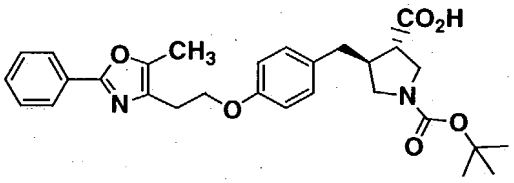


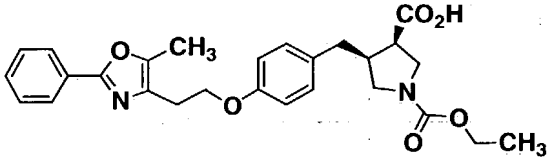


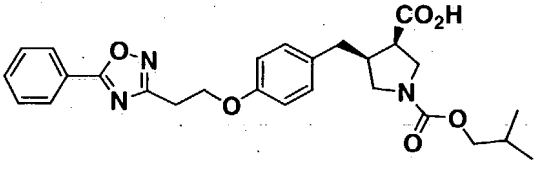


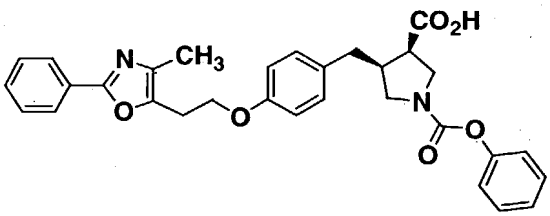


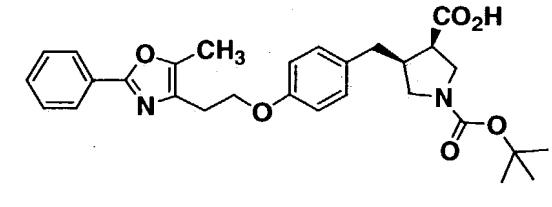


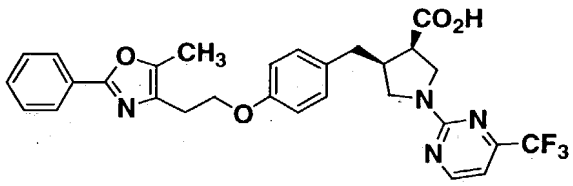


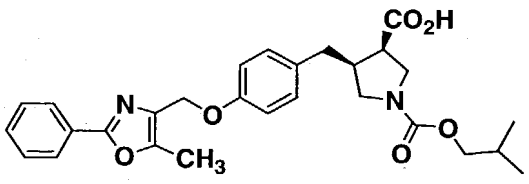


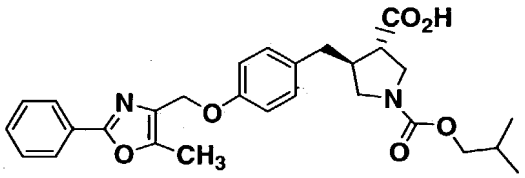


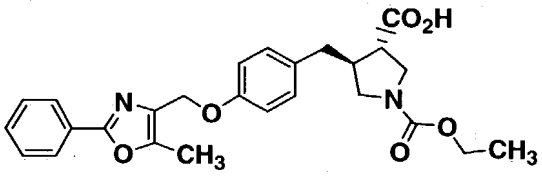


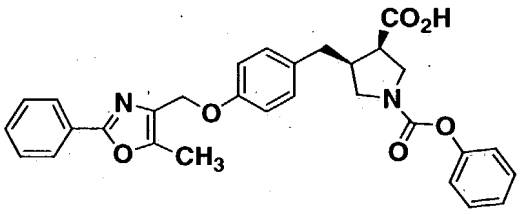


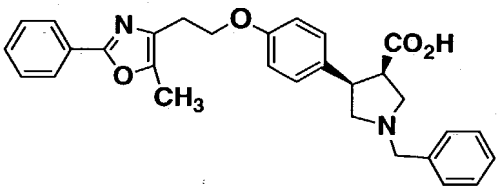


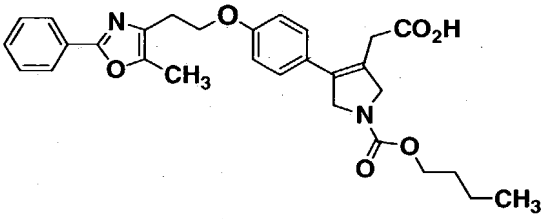


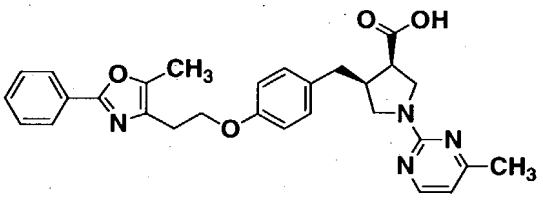


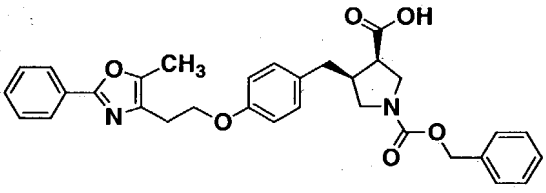


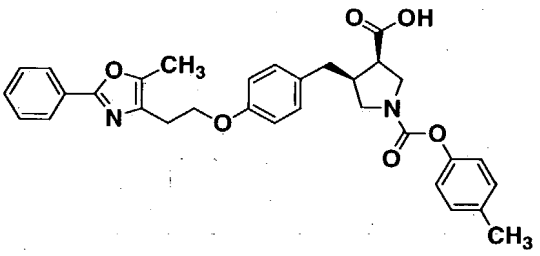


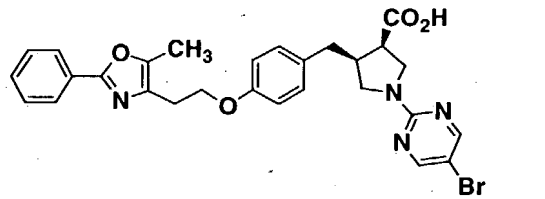


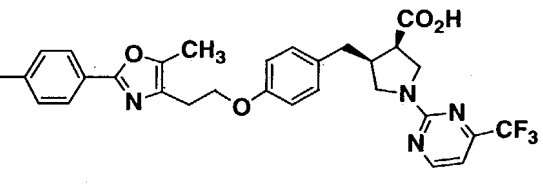


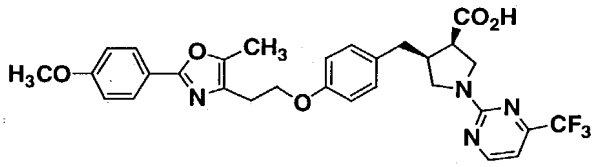


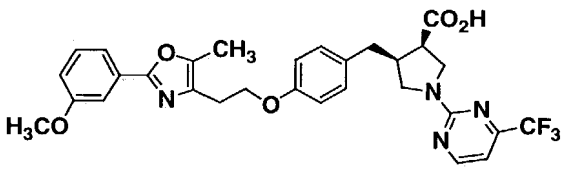


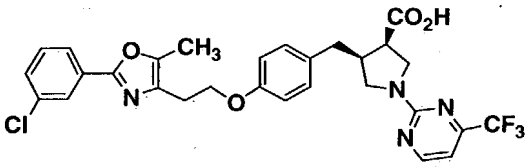


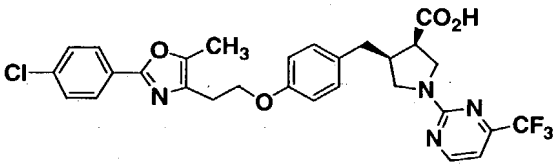


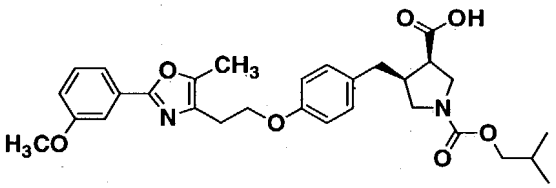


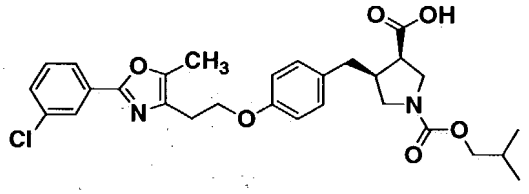


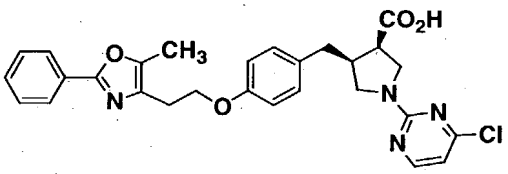


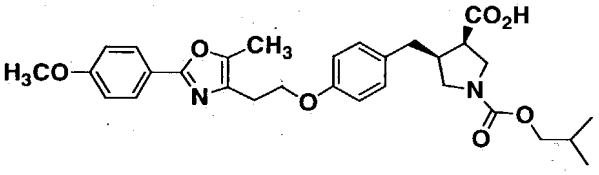


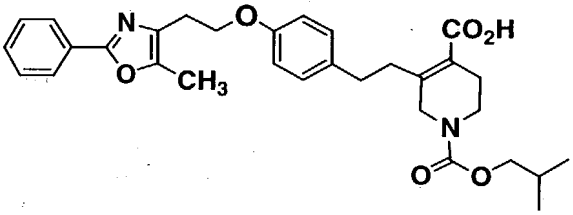


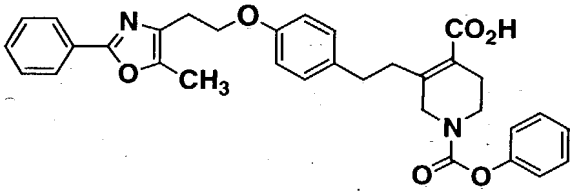


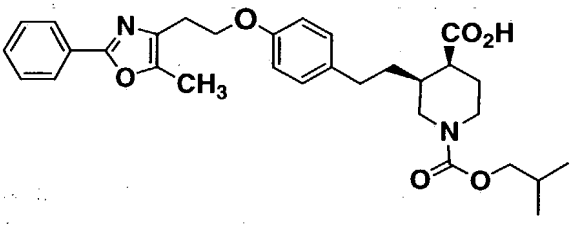


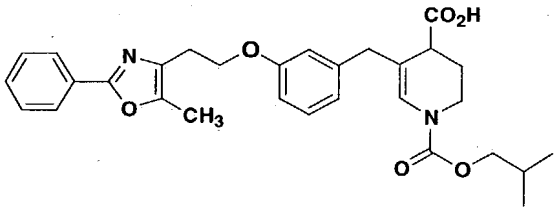


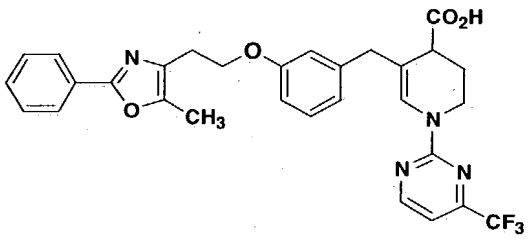


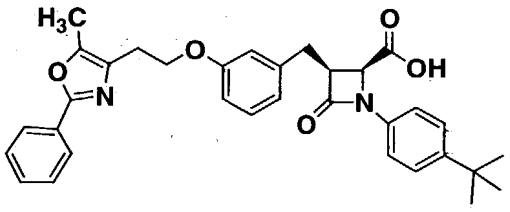


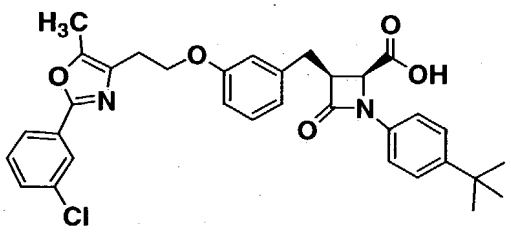


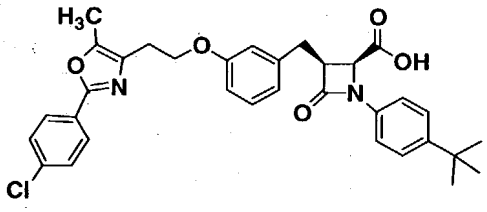


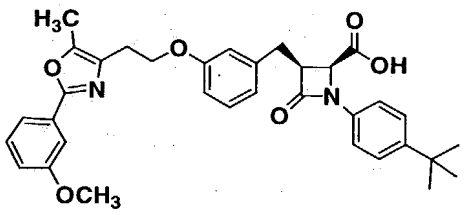


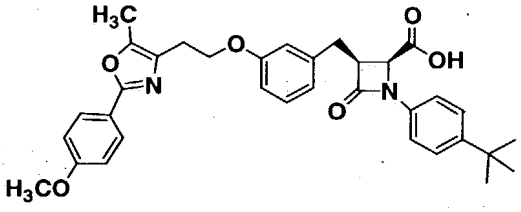


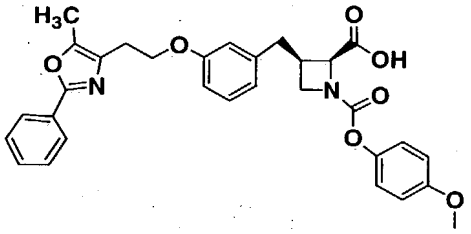


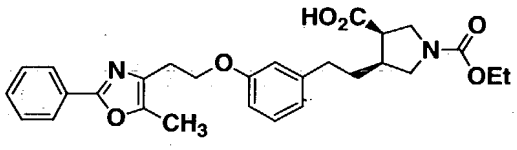


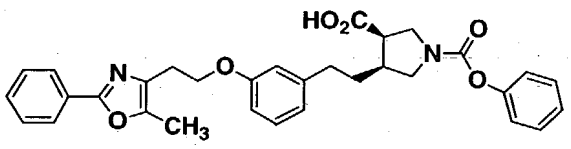


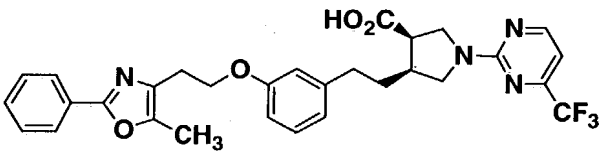


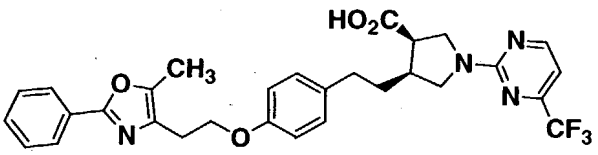




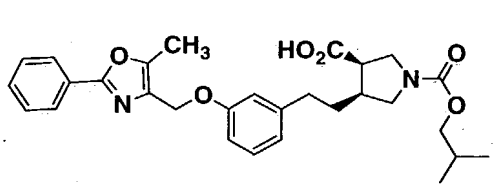


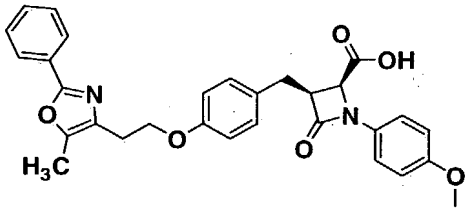


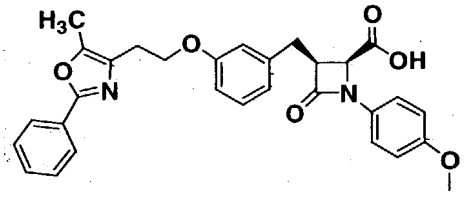


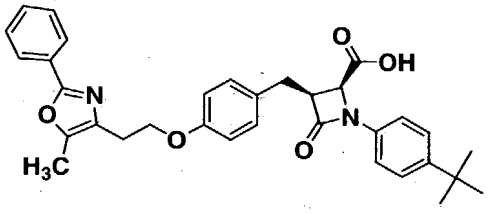


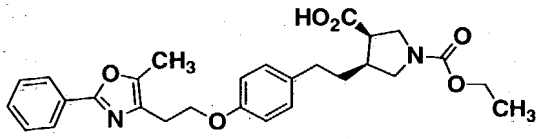
- 539 -

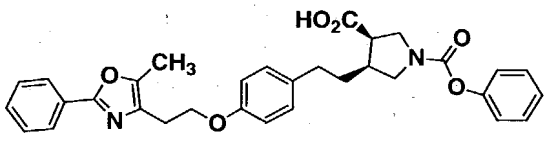












14. A pharmaceutical composition comprising a compound as defined in Claim 1 and a pharmaceutically acceptable carrier therefor.

15. A method for treating diabetes, especially Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, atherosclerosis, and related diseases, which comprises administgering to a patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

16. A method for treating early malignant lesions (such as ductal carcinoma in situ of the breast and lobular carcinoma in situ of the breast), premalignant lesions (including fibroadenoma of the breast and prostatic intraepithelial neoplasia (PIN), liposarcomas

and various other epithelial tumors (including breast, prostate, colon, ovarian, gastric and lung), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and osteoporosis and proliferative diseases such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

17. A pharmaceutical combination comprising a compound as defined in Claim 1 and a lipid-lowering agent, a lipid modulating agent, an antidiabetic agent, an anti-obesity agent, an antihypertensive agent, a platelet aggregation inhibitor, and/or an antiosteoporosis agent.

18. The combination as defined in Claim 17 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR γ agonist, a PPAR α/γ dual agonist, an SGLT2 inhibitor, a DP4 inhibitor, an aP2 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin and/or a meglitinide, the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor agonist, an aP2 inhibitor, a cannabinoid receptor-1 antagonist and/or an anorectic agent, the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, a farnesoid receptor (FXR) agonist, a liver X receptor (LXR) agonist, a CETP inhibitor or an ACAT inhibitor, the antihypertensive agent is an ACE inhibitor, angiotensin II receptor antagonist, NEP/ACE inhibitor, calcium channel blocker and/or β-adrenergic blocker.

19. The combination as defined in Claim 18 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, rosiglitazone, balaglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AZ-242, AC2993, LY315902, P32/98 and/or NVP-DPP-728A, the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, rimonabant (SR-141716) and/or mazindol, the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, fluvastatin, itavastatin, visastatin, rosuvastatin, pitavastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, ezetimibe, TS-962, MD-700, cholestagel, niacin and/or LY295427, the antihypertensive agent is an ACE inhibitor which is captopril, fosinopril, enalapril, lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril; an NEP/ACE inhibitor which is omapatrilat, [S[(R*,R*)]-hexahydro-6-[(2-mercapto-1-oxo-3-phenylpropyl)amino]-2,2-dimethyl-7-oxo-1H-azepine-1-acetic acid (gemopatrilat) or CGS 30440;

an angiotensin II receptor antagonist which is irbesartan, losartan, telmisartan or valsartan;

amlodipine besylate, prazosin HCl, verapamil, nifedipine, nadolol, propranolol, carvedilol, or clonidine HCl, the platelet aggregation inhibitor is aspirin, clopidogrel, ticlopidine, dipyridamole or ifetroban.